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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/657,516	09/08/2003	Francois Binette	022956-0225	7793

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EXAMINER	
BERTOGLIO, VALARIE E	
ART UNIT	PAPER NUMBER
1632	

NOTIFICATION DATE	DELIVERY MODE
05/18/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

docket@nutter.com

Office Action Summary	Application No.	Applicant(s)	
	10/657,516	BINETTE ET AL.	
	Examiner	Art Unit	
	Valarie Bertoglio	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 August 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *48-69* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *48-69* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *08 September 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *01/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The instant application is now under examination by Valarie Bertoglio, AU 1632.

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 08/18/2008 has been entered.

Claims 1-47 are cancelled. Claims 60-69 are added. Claim 48 is amended. Claims 48-69 are pending and under consideration in the instant office action.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The rejection of claims 48-51 and 54-56 under 35 U.S.C. 102(b) as being anticipated by Glorioso et al (6,413,511; IDS) is withdrawn in light of Applicant's amendments to the claim requiring that the substrate have a length of 10cm-30 cm.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 48-51 and 54-56 are rejected under 35 U.S.C. 103(a) as being unpatentable over Glorioso et al (6,413,511; IDS).

Glorioso et al. disclose a chondrocyte that encodes a polypeptide of interest including interleukins, cytokines, tumor necrosis factors and biologically effective fragments thereof, which can be delivered to articular cartilage (see col. 27, lines 59-65, col. 21, lines 10-37). Glorioso also disclose that said chondrocyte can be delivered with a gel matrix substrate to the damaged tissue site (see 29, lines 13-16). Glorioso further disclose that delivering a therapeutic agent to the damaged joint to treat arthritis (which can be an autoimmune disorder, see col. 27, lines 35-65). A recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In the instant case, the intended use of the chrondrocyte does not impart a structural difference with what's disclosed in the prior art. Glorioso does not teach use of a substrate having a length of about 10cm to 30 cm.

However, Glorioso does teach making a larger than necessary biocompatible substrate and cutting the substrate to fit the implant site (column 46, lines 42-43). It would have been obvious to make a large 10 cm long implant to either accommodate a larger lesion, to provide a large enough implant that a piece can be cut to fit an implant site, or to cut multiple implants from the same larger substrate. The increase in composition length fails to impart novelty on the claimed composition as it would have been obvious to one of skill in the art to make a larger composition for reasons set forth above. Using a substrate which could then be used to cut multiple, custom sized substrates would be fully within the skills and knowledge of the ordinary artisan. One of skill in the art would have a reasonable expectation of success in making a larger biocompatible substrate as a larger substrate would merely comprise more of the same product.

Additional claim limitations added to claim 48 fail to impart any novelty or non-obviousness to the claimed composition as they are related to the intended use of the claimed product. Applicants are reminded that the claimed invention is directed to a product, the modified chondrocyte, rather than a process, such as a method of using the chondrocyte as a delivery vehicle to a site that is foreign to chondrocytes. As stated before, the intended use of chondrocyte would only be considered a limitation that distinguish from the prior art if it makes a difference to the structure of the claimed chondrocyte. However, in the instant case, the limitation of "wherein the target region is an ectopic site...and is not used for tissue repair or construction" does not impart a structural difference of the claimed chondrocytes to the chondrocytes disclosed by Glorioso.

Claims 52-53 remain rejected and newly added claim 60-64 and 69 are rejected under 35 U.S.C. 103(a) as being unpatentable over Glorioso et al., as applied to claims 48-51 and 54-56 above, and further in view of Bartholomew et al. (Human Gene Therapy, 2001, 12:1527-1541; IDS).

The teachings of Glorioso are newly applied to claim 48 as set forth above.

Applicant's arguments regarding the teachings of Glorioso are addressed above.

Applicants argue that Bartholomew does not teach or suggest using a biocompatible substrate in place of the IID's to deliver genetically modified cells or EPO mimetibody. Applicants further argue that Bartholomew fail to disclose the use of genetically altered chondrocytes for expressing EPO or its mimetibody, or the ability of the modified chondrocytes to express the therapeutic when delivered at an ectopic site. Applicants thus conclude that the claimed invention is not obvious in view of the combined teaching of Glorioso and Bartholomew.

Applicant's arguments have been fully considered but deemed unpersuasive. The detailed reason for this rejection was set forth in previous office action. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the

rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). It would have been obvious to one of ordinary skill in the art to express erythropoietin or erythropoietin mimetibody in the chondrocyte taught by Glorioso et al. and combined with a biocompatible substrate based on the general knowledge in the art at the time of filing. The claimed invention would have been obvious because the substitution of one known element for another would have yielded predictable results to one of ordinary skill in the art. As evidenced by the teaching of Glorioso et al., one of ordinary skill in the art would have reasonable expectation of success in introducing a transgene into chondrocyte and express said protein *in vitro* or *in vivo,* and following the guidance of Bartholomew, one of ordinary skill in the art would have reasonable expectation of success in introducing the coding sequence of human EPO or mimetibody into a vector and express it *in vitro* or *in vivo.* Therefore, the invention would have been *prima facie* obvious to an ordinary artisan at the time the invention was made. It is not suggested in the rejection that the chondrocytes of Glorioso be substituted with the MSC of Batholomew as suggested by Applicant. Furthermore, Bartholomew is not relied upon for teaching a genetically altered chondrocyte. Glorioso et al. discloses that chondrocytes may express a polypeptide of interest including interleukins, cytokines, tumor necrosis factors and biologically fragment thereof. EPO is a cytokine for erythrocyte precursors in bone marrow. While the nucleic acid sequence that expresses EPO is known at the time of filing, substituting the transgene transfected to the chondrocyte as disclosed by Glorioso with construct expressing EPO or fragment thereof would have yield predictable results to one of ordinary skill in the art, wherein the result is expressing EPO in said chondrocyte. KSR forecloses the argument that a specific teaching, suggestion, or motivation is required to support a finding of obviousness. As such, based on the combined teaching of Glorioso and Bartholomew, an ordinary skilled in the art would realize that all the claimed elements were known in the prior art at the time of filing, and would have combined the elements as claimed by known methods with no change in their respective functions, and the

combination would have yielded predictable results to the ordinary artisan at the time of filing. Absent evidence from the contrary, the claimed invention would have been *prima facie* obvious in view of the teaching of Glorioso and Bartholomew at the time of filing.

Claims 57-59 remain rejected and newly added claims 65-67 are rejected under 35 U.S.C. 103(a) as being unpatentable over Glorioso et al., as applied to claims 48-51 and 54-56 above, and further in view of Okada et al.

The teachings of Glorioso are newly applied to claim 48 as set forth above.

Applicant's arguments regarding the teachings of Glorioso are addressed above.

In response to this rejection, Applicants argue that Okada fails to teach use of genetically altered chondrocytes.In response, Glorioso is the primary reference relied upon for meeting this limitation. Okada is relied upon merely for teaching the additional limitations of claims 57-59 and 65-67.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Valarie Bertoglio whose telephone number is (571) 272-0725. The examiner can normally be reached on Mon-Thurs 5:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on (571) 272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Valarie Bertoglio/
Primary Examiner, Art Unit 1632